Zan Fleming (00:10:04):

Well, we are at the top of the hour, I want to say good morning and good evening to our global audience coming in and around Washington dc It's the eighth annual Wow. Or Yale or holy cow, FDA and review. And look ahead. As usual, we have a preeminent panel, but an unusually long list of hot topics to cover many in the holy cow category. And by the way, Tim Franson gave us that technical term, which I think is very apt, but Thomas, over to you for some housekeeping notes.

Thomas Seoh (00:10:50):

Thanks, Zan. A housekeeping reminder to enter any questions for the speakers in the q and a function of our Zoom webinar platform and the panelists will try to get to them as time allows. As usual, a link of this recording will be circulated to all registrants and made publicly available within the next day or two. A distinctive feature of our virtual conference sessions is that we enable the chat function for audience interaction. So just for warmup, for those of you who are willing, please say hi in the chat, your affiliation of desired and from where you're logged in now, turning the mic over to connect some founder and executive chairman, Dr. Alexander Fleming Z.

Zan Fleming (00:11:27):

Well, thanks Thomas. We are so honored to have join us, Dr. Janet Woodcock, who perhaps more than any single person has shaped therapeutic review and regulation at FDA over close to four decades. And no one could get us started better with Janet than Frankowski, who's the dean of rare disease therapeutic development, and a master strategist across multiple therapeutic areas. So Frank, I'm going to turn it over to you to get us started with Janet.

Frank Sasinowski (00:12:02):

Thanks, Zan. And it's just a pleasure to welcome you, Janet, to this panel. We've been doing this under Z's leadership for eight years now. This is our eighth and obviously because last year at this time you were still at the government, and so we call it the WOW or Yao. And I'd have to say it's a tremendous Yao that on January 26th, 2024, we lost you after nearly four decades chose your opportunity to have these kind of fireside chats. And I thank you for having the fireplace behind you so we can get started. So when Bob Temple, our common friend, good friend, retired in December, the BioCentury headline said, father of the modern FDA, I think that they should have said that when you retired, you were the mother of the modern FDA. I don't know what Roger or Bonnie would think about the two of you being the mother and the father, but I think you are the mother of the modern FDA. So thank you for being here with us. A first question is that right after, not long after you retired, you gave me a call, said, Frank, I'm calling you from the matriarchy. I said, what's that? You said, I'm calling from Santa Fe, New Mexico, a high end resort. I'm meeting with the women CEOs of biotech, and we have a question about rare disease pathway. And so I'd like you to talk a little bit about one of the first things I heard you get engaged with after your retirement.

Janet Woodcock (00:13:35):

Thanks, Frank, and happy to do so. Yes, I'm working on trying to get another variation to the way that you can show substantial evidence. And I thank Dave Fox who's on this panel for his intellectual contributions to this because they were substantial. We have had, over the years, first we had two adequate and well controlled trials, and that's what Bob spent 20 years establishing and in the courts and so forth in P lesson 0.05 and all this kind of stuff. And that was really good. That was a triumph because we had evidence-based drugs getting on the market, but then we had the AIDS crisis, we FDA

invented accelerated approval. They had had numerous large trials with survival advantage, and it was, you can't really, are we going to enroll people in a placebo and do a second trial when we showed that? And so we had single trial plus confirmatory evidence.

(00:14:36):

So that was another variation along with accelerated approval. And then when bioterrorism became a big concern, we had the animal role, which FDA published the first two Congress instantiated eventually in statute. The other one is a role, the animal role whereby FDA can approve things based on animal model studies when human studies aren't feasible. Now, what turns out though is a randomized controlled trial is not fit for purpose for small heterogeneous populations. And we've seen this over and over again, and we've seen that about maybe 1400 rare disease programs have been paused in the last few years because there is no feasible way forward. So the variation I'm seeking is that for smaller populations, heterogeneous populations in particular where the RCT isn't feasible, other trial designs should be acceptable. And you might say, and I'll stop talking soon, but you might say, well, FDA's already done this.

(00:15:43):

That is true, but it's inconsistent. It's not predictable. And so it isn't as if you can rely upon that and go forward and design a program. And frankly, between the agency and companies, they spend years struggling over how to design A RCT type of trial. And what they should be doing is sitting down and talking, how can we generate convincing evidence? How can we do that? And I have ideas, of course, always have ideas about trial designs that would do that. So I'm working on that. I'm working with the Haystack Project, and we're going to have a technical workshop just on the design issues in a couple of weeks and hopefully move forward. So thanks for asking.

Frank Sasinowski (00:16:28):

No, thank you. Because that's an area I've been working on too in my career. So I just welcome having your voice in this process. And because you have a voice that has a lot of influence, you speak with a great authority. And so I can be a voice crying in the wilderness, but it's good to have you on board and moving this forward. So thank you. Well, Frank,

Janet Woodcock (00:16:53):

I think it's a technical problem and we need to move it from advocacy problem to technically these RCT doesn't work the P value less than 0.5. You have to have a miracle. If you have 60 people to randomize who are heterogene, you'd have to have a miracle to have a miracle drug. But for headaches or for all kinds of stuff, you can roll a lot of people and have only maybe 10% of the people benefit. And it's effective, right? But for rare diseases, you have to practically have a cure. Is this fair when these are the people who are suffering so badly? Many of them. So I'll stop there. No,

Frank Sasinowski (00:17:37):

No, but that's beautiful. I'd love to have you go on with both. But you also, you've been called the Renaissance woman because you've been involved with so many things inside the FDA. Let's move to, what about your role in improving pharmaceutical manufacturing? Where do you see that?

Janet Woodcock (00:17:54):

Yes, I am still working on that. I'm working with Anders and he's been putting on quality business leadership training over in Dublin. And this is going pretty well, I think, to move the quality people up.

I'm also, and I can't necessarily talk about it, but I'm working with, I've decided that big pharma and the generics, neither of them are going to push on advanced manufacturing. So I want to work with the contract manufacturers because they will have a clear vision that this is a competitive advantage, right? If they can do it right. So yeah, I'm still working on this because people talk about bringing manufacturing back to the United States, having more redundancy and everything, but what are we doing about it? And I would think the only way you could really do that and bring manufacturing back and actually put it different places is to use different manufacturing techniques than what is commonly used today.

Frank Sasinowski (00:18:54):

Thank you, Janet, for all that work. So what else have you been up to?

Janet Woodcock (00:18:59):

Well, I don't want to dominate. I don't want

Frank Sasinowski (00:19:01):

To talk about your gardening. No, no, no.

Janet Woodcock (00:19:03):

Okay. Or my orchids. Yeah, no,

Frank Sasinowski (00:19:06):

Don't go there.

Janet Woodcock (00:19:07):

Okay. Well, I am working on a project with RA Capital up in Boston, and it's partly for rare diseases, but not totally What it is is trying to get an AI driven diagnostic interview for patients that would give them a differential diagnosis linked to patient advocacy organizations of diseases that they might have linked to resources, tell them what kind of tests and workup they should have because so many people are misdiagnosed not just with rare diseases but common diseases. But what is missing in my mind is the link between the patient and their lived experience and what goes in the chart, a medical lingo, and there's this giant gap there. And so the AI have a lot of translation functions, but we've never trained AI on how patients talk about their disease. So that's what I'm going to do or I am doing.

Frank Sasinowski (00:20:07):

No, that's fascinating. Hey, z, I think that we were going to have this little introductory fireside chat just to get us going. So why don't I back over to

Zan Fleming (00:20:17):

You. Well, thanks Frank. That was great. I love that dialogue. And we're going to come back to Janet for some selected topics a little bit later, but why don't we now go to Steven Grossman, who has been what I would call the FDA advocate in chief and his very effective role as executive director of the Alliance for a stronger FDA. And Steven was just feted last night to thank him for that service. But Steven has left very important fingerprints on a lot of things. FDA, although he never served in the agency, but for

example, was involved with the Orphan Drug Act back in the early eighties. So Steven brings a terrific purge, and Steven glad you could rejoin the panel this year.

Thomas Seoh (00:21:16):

You're on mute.

Steven Grossman (00:21:23):

Okay. I did want to correct one thing. I did work at HHSI was in the level above FDA and I learned how little they wanted to be controlled by downtown DC

(00:21:38):

For everybody who served at the agency. That should resonate. That's really my first taste, was there and made a lot of good friends, learned a lot in the process of trying to avoid FDA evasion from the Assistant Secretary for Health. I think the part I've been assigned is to look at some of the institutional issues. Transitions are always a difficult time, and it's true whether it's a friendly transfer or an unfriendly transfer. And several, the people like Janet have seen both. But every new administration, even if the prior administration was of the same party, want to put their own mark on things. And that's what we're seeing. And the cases, if you go back to each of the change of control elections, change of president, you see a degree of uncertainty that starts with somewhere in December usually and go continues at least through May.

(00:22:52):

Historically, the last two people who were nominated at the beginning of a new administration were, their names were announced in early March and they were confirmed in May. So my choice of say June one is not entirely arbitrary. This administration got started by naming someone much, much earlier. But as far as I can tell from people, late February, early March is probably the likelihood for a confirmation hearing. So maybe we'll see a commissioner closer to April one than in the past. Meantime, we have a large number, a massive number of executive orders and other things that are affecting FDAI made this point a little earlier with a much smaller organization audience. I'll make it again, there is no question that the sum of all these executive orders is to dispirit the federal government workforce and to encourage people to retire, leave service. In some cases that might be premature.

(00:24:11):

In other cases, it may be the number I saw, and Janet probably knows a better number, is that about 15% of the FDA workforce is retirement eligible. And when you look at how people are going to make decisions, there's a huge difference between, I wasn't expecting to retire today and I'm not sure what I do next and being retirement eligible so that if you figure, because I know we'll get back to brain drain, but if you just do the math, say a one quarter take up on retirement eligible people, that's probably about a thousand positions right there before you get to all the other stuff. The larger point is that because FDA has multiple personnel systems, multiple sources of revenue, a much larger range of job positions than most agencies, as we're getting each of these top down announcements about retirements, about return to work, they all apply in general to FDA, but you should not assume immediately that they had the same impact as either was intended or the same impact as they might have on some other agency because of the different personnel systems, as some of you have lived through shutdowns know for instance, the only FDA employees that work through a shutdown are the Public Health Service Corps members because they technically are presidential appointments and not personnel.

(00:25:55):

So that's just an example. That's not necessarily what's happening today so much as an example of how the variation is so great. I was asked to address a couple of institutional issues. One is that I've started a new newsletter called FDA Matters, and one of the columns was called Keep Calm and Carry on Title I owe to Xan. Thank you. And I think that's the most important advice right now. No one does really know what's going to happen a month, six months from now, and people should not let their imagination run. Wild. FDA has survived a lot of changes, a lot of turmoil. It's not good. I'm not for turmoil, but it is also the case that it is an agency that does survive and it's in all of our interests that people not jump to conclusions and that people not decide before they know what's really going to happen. It's one thing to worry about the management you're going to have. It's quite another to wait and see because that often does work out. And this interestingly enough, was also advice that Dr. Califf was giving people. So to me, the standard becomes these are going to be hard times in a lot of ways and the agency is going to survive. And I think the main thing is for all of us to be sure that the people stay together because FDA is the people.

(00:27:35):

When everybody goes home, there isn't really much going on compared to other operations. So that's one point that I want to make as a threshold. Just take a deep breath or as Z said, keep calm and carry on. A couple of other things I was asked about to comment on was the McCarey confirmation, and especially as we're in the midst of the Kennedy confirmation hearings, I can just give my view on the McCarey one, which is he's qualified. If you look back over, and I'm now on my 13th or 14th commissioner, I think I'm even head of Janet on that one, but probably not the head of Frank.

(00:28:24):

Everybody brings a different style. Everybody brings different strengths. Well, within the range of people who held the office, I think for most of us, the most important question is, and maybe we'll know a little more confirmation, is whether he's going to be willing to stand up to orders that are not necessarily in the best interest of the public, not necessarily in the interests of FDA, that may be anti-science. I think it's safe to say every commissioner, regardless of who they are or who their boss is, faces this. And somebody at the reception last night made an interesting observation. I said, well, that's the key question. Is he going to stand up and say no? And they're responsible even he probably doesn't actually know yet. And that's consistent with my experience. And each of us who's had a role in government, which is a lot of things you think about and you say, well, I'm going to do this, I'm going to do that when the moment comes.

(00:29:26):

And so I think we'll know more after the confirmation, but the moment of truth really comes after that. Two other things, the resources, the resources, constraints on the agency are already not good. It's not just is there money to pay for personnel, but there's dire need for new computer systems, new it, ai, everybody. There's a lot of talk about AI in terms of applicants applications and companies, but one of the most important issues for FDA is how can they use AI to make better regulatory decisions? And at least at the moment, I don't think there's any money for that and that needs to be. And then there's the largest struggle, which is Congress is going to be looking at a lot of across the board cuts where individual agencies mission importance are not going to be examined one each agency. And that's an important thing.

(00:30:29):

My success with the alliance for stronger FDA CAR esham is wonderful, and she's going to be one of the point people on making sure Congress understands that FDA is different and needs different treatment.

And then finally, the last thought I had was on making Americans healthy again. And the reason I think it's important is you've heard Janet reference, we're all always aware, there's always a struggle to find the right standards for approvals. And food of course operates very differently. But I think we all need to see that this is going to be as profound battle for the food industry and for food stakeholders and for each of us as Americans, as what it is constitutes to take to having a drug approved and that it's going to draw all of us in. I think that's good. There's lots of questions that need exploring. I think there are going to be a lot of uncomfortable stuff. I do think that in its own way it's going to be a bigger deal because food is more personal and it's more relatable for people. And you're going to have people who would never dare to have an opinion about drug approvals who are going to have an opinion about maha. So anyway, that's just some institutional thoughts.

Zan Fleming (00:31:53):

Well, terrific Steven, and we will come back to Janet to talk about food because that became a passion of hers in her latter tenure at FDA. And so she will definitely be able to speak to us about issues there. But let's now go to Kate Rossin who is I believe one of the most effective journalist of FDA matters and incisive in her approach to the issues that FDA with her broad perch. She can certainly cover a lot of FDA territory. So Kate, let's start with your first thoughts.

Kate Rawson (00:32:37):

Yeah, Zan, thank you so much and I'll make some brief remarks. And then I think I saw Janet coming off mute, so I'm sure she's going to have some things to respond to as well. So first, I mean we could talk all day about this transition, but I'm going to try to keep my remarks really succinct and build off of what Steve has already said. And I agree the sky is not falling, but it looks kind of dark out there. I got to say we've had this triple punch of the communications freeze, the mass retirement offer and the return to work directive that really sent based on conversations that we've had with folks, the agency staff into a bit of a tailspin this week. And that's really not an overstatement. That retirement offer, which was entitled to work in the road, which I sort of smiled at, was emailed really to everybody as we know at F FDA A and all federal agencies with some exceptions.

(00:33:41):

And the directive was just to simply respond with resign in the subject line. They would then be exempt from these return to work directives that I think take effect on February 20th and not work, but in most cases, but continue to be paid through September 30th. I think the legality and the attractiveness of that buyout plan is still not clear. Like Steve said, there's a lot we don't know. I think the broader point obviously is that the Trump team is following through on its plans to significantly reduce the size of the federal workforce. That's not terrible except I'd add that that offer went out to everybody, including senior leadership and including people that you wouldn't want necessarily want to leave FDA because it would be so disruptive. And just as a reminder, I know brain drain has been thrown around a little bit. I know everybody was worried that the sky was falling. Janet when you retired. We're seeing, we've already seen some other high profile recent departures that some that probably were not related to the oncoming administration and others that feel like they probably were like our former Cedar director.

(00:34:56):

On top of that, the administration is also looking, and this is what we're watching, is looking to target other people that maybe the administration doesn't believe supports President Trump's personal views on issues like vaccines or abortions. In that one of the many executive orders that came down on the 20th, he stripped employee protections for, I've seen estimates of at least 50,000 career employees that

would effectively make them at will employees. That plan has already been challenged in court, so it may not hold up, but I think it does, as we said in our intro when we were making our intro remarks that it casts appall over the agency and that was probably the point from the beginning.

(00:35:55):

It's also hard when your and Janet made this point when we were sort of chatting informally, when you can't send an all hands memo or talk to your staff in a group as a group, that's hard. That's hard for leaders, that's hard for reviewers, that's hard for the staff. At the same time as a reporter, I can't help but notice that there have been no real press releases coming out of FDA since Inauguration day with some exceptions. And to be clear, the work is continuing. We are seeing approvals be announced by industry, although I can only imagine how distracted the staff has been during this time. But FDA has not been allowed to publish press releases or update websites. I think that the good news is that that freeze appears to be starting to thaw. There was a press release yesterday about a non-opioid pain medicine from Vertex, and there were other releases today that weren't as high profile.

(00:37:00):

So it makes one think that maybe things are starting to open up, but at the same time, we're seeing on a systematic takedown of any websites or programs that remotely address DEI issues. FDA Office of Minority Health is down the oncology center for Excellence's project equity program. It's down any guidance related to clinical trial diversity, including all the work that industry and agency staff have put into diversity action plans. So a generous reading of this is that the administration is just reviewing all that DEI work and we'll reinstate some of the programs. We'll see. Again, we don't know, but I would submit that there are two really big questions related to the DEI down. And the one is that that requirement for diversity action plans was codified in law under fedora. So I'm sure if there hasn't been already litigation over whether the administration can simply decline to publish the final guidance called for in the statute.

(00:38:04):

But I would also submit that this situation is very challenging for biopharma sponsors who for the past four years have been working on DEI have been encouraged to open DEI offices and have been submitting diversity action plans in recent months to the agency to get out ahead of this and to understand what the requirements are going to be. I think President Trump has clearly said that he hopes that companies will follow his anti woke agenda against DEI and that could complicate things for industry because as a practical matter, drug developers still need to address questions or concerns about diversity of clinical trial populations. They need to enroll a diverse patient population to both represent where the disease is most prevalent and understand potential signals of different responses in different subgroups. So there are some potential implications for the future of clinical trials in general, not ones that are running right now, obviously, but ones that could be planned. And that's something that we certainly think that we will be continuing to follow. Interestingly, in his confirmation hearing this week, RK JR did pledge to continue work on the diversity action plans as mandated by Congress. I don't assume he understood that question. There was some confusion during that exchange as to whether he knew what they were and he might not. Just as the HHS nominee, you're not going to know everything about everything. But he did make that commitment, at least in the, I think it was the Senate Finance Committee hearing.

(00:39:43):

The other thing I was asked to talk about was just I do want to share some observations from the nominations hearings this week for RFK Junior. There were back to back hearings in the Senate Finance and in the help committees, and they really did underscore a definite sort of anti pharma and

sometimes anti FDA sentiment from our potential HHS secretary. So I think just really briefly, a couple of key themes over medication comments that were made by the nominee are a risk for pharma. He repeatedly stated that this claim that pharmaceutical drugs are the third largest cause of death in the us and we think the risk there is that his views on overmedication will soon be sort of orthodoxy in the Republican party in the same way that once these fringe anti-vaccine views have now been moved into the mainstream, he did sow some doubts about specific drug classes.

(00:40:49):

He specifically targeted antidepressants, for example, as being over-prescribed and dangerous. And then we saw a tweet from Elon Musk to that effect as well. He's called into question Alzheimer's disease research based on the amyloid plaque reduction work there, we saw not a lot of moderation in his vaccine views. It felt like maybe the older vaccines were safe, but he repeatedly declined to say that the MMR vaccine does not cause autism. He defended the position that the HPV vaccine Gardasil leads to an increase in the risk of cervical cancer. He questioned whether covid vaccines save lives, and he described HH S'S network of vaccine surveillance programs as hopelessly flawed. And then he also did on the other hand, appear to support some specific interventions like the GLP ones appeared to generally support their use in obesity with some caveats and then also supported medically assisted treatment for opioid use disorder. So those were sort of our takeaways from about six hours of testimony this week. I'm going to pause there. I have some other topics that I've been assigned, but I'd love to hear any responses from what has been said already or we can move on to other topics.

Zan Fleming (00:42:14):

And Kate, we'll give you a few seconds to end on what you would see as a bright spot cell and gene therapies.

Kate Rawson (00:42:20):

Yeah, no, I think cell and gene therapy, it's an exciting IT area of development. I think if SIBER and OTP can kind of keep its head down, there's a lot of great stuff down the road for cell and gene therapy development. I think with all the covid work, obviously now behind it siber, there may be some critiques that they're going to have to deal with. But siber seems to be firing on all cylinders now with cell and gene therapies. I think Peter Marks as the director of siber is enthusiastic about using accelerated approval for gene therapies to speed up development. There's a near term promise of using AI to take out the bumps in gene editing in the gene editing manufacturing process. We've had three regenerative therapy approvals in 2024 and just two in December, which sort of plow this nice path for future development. And hopefully I hope that enthusiasm around cell and gene therapy development will keep OTPs engaged and in their seats. And I think still to be determined, and I'd love to hear what Frank thinks about this and Janet too, the impact of the two-headed siber cedar rare disease hub, especially without a permanent C director at the moment. But exciting times ahead for cell and gene therapy for sure.

Zan Fleming (00:43:44):

Well, terrific. We'll come back to that in a moment, but let's go on to Tim Franson and many thanks Kate. That was wonderful. Terrific summary. Tim Franson, master drug developer, former formerly at Lilly, an infectious disease specialist and a professional punster who often adds to our humor in this session. Tim, let's start with issues related to pediatric trials and what you have termed pediatric trials and tribulations. Take it away. Thanks

Tim Franson (00:44:23):

And it's a real privilege to be on a panel with folks that I respect and have enjoyed collaborating with over the decades as it relates to pediatrics. It said that the humanity of a culture can be judged on how they treat their most vulnerable, especially children. And one would have to challenge at this point whether we're doing enough for the best health interests for our youngest constituents and what that means for the future. So let's talk about the practicalities. If you fast rewind to where we were with PDUFA two and the provisions for pediatric exclusivity at that point in time, development of compounds for children were very minimal. And without those incentives, we were seeing up to 90% of, for example, oncolytic drugs that were not labeled for pediatric use. Those are not flattering figures, it's not scientifically driven. And as a result of those incentives with BPCA and PREA and incentives for pediatric drug development, there have been several studies that talk about three to 400 compounds that have now been labeled for pediatric use.

(00:45:47):

That's an incredibly good news story. It's appropriate in many ways for not only practitioners but policymakers, but let's now look at the more recent circumstances where a number of pediatric research centers have been either closed or minimized Tufts being a particular example. In that regard, the training of pediatric investigators for clinical trials has been truncated. Several major pharmaceutical companies have closed their pediatric trial groups, and those are not encouraging when you look at the fact that the need for pediatric therapeutics, especially for acute diseases, we've done a huge shift to chronic with adults, but the great threats to our pediatric population come frequently from acute diseases and nowhere has that been more evident than with infectious disorders. Speaking as an infectious disease physician and as a grandfather, I'm convinced that we need to have new incentives as FDA has deemphasized the BPCA provisions and incentives and perhaps that's appropriate.

(00:47:07):

They may be outdated and we should be revisiting the ways to catalyze drug development for pediatrics at these points in time. But I would submit that our children in America are disadvantaged immunologically because especially as in neonatal populations, they don't have mature immune systems societally, there are a number of things that conspire such as food insufficiency and a significantly large minority of children's populations. So we're essentially setting kids up for the likelihood of not responding well to infectious disorders. And that culminates with the recent vaccine declines. And we can speculate about the political reasons, but I would argue the medical are much more important. We're now seeing recurrences of diseases such as whooping cough and measles, which are certainly highly contagious. There are reasonable treatments for whooping cough, borella pertussis, but not so much for measles. And some of us who trained in environments around communities that had religious preclusions on vaccine use have seen the natural experiment of what happens when you aren't immunized against measles, blindness, loss of hearing, encephalitis, not very pleasant things. And when you talk about that being totally preventable, this becomes very worrisome because the public has an eroding confidence in science in vaccines. And those things are quite distressing when you think that this disadvantages the young and it's entirely inconsistent with our scientific base. So sorry, I don't have anything humorous or punny to offer in those areas, but I do think that we should take a note of positive and that there'd been no proposals to repeal the law of gravity because without it, we'd have nothing to stand on.

(00:49:22):

And Zan, you had several other topics provided for me. I don't want to leave it without. What can we do? There are a number of incentives I think we can reinstitute that will help us with pediatric drug

development. I think the pediatric rare disease priority review voucher is a program that sits now in limbo and is a great opportunity of being renewed if we all put our shoulder to the wheel on that. And I know we were going to talk about pandemic elements. Would you prefer I holt for a period, catch breath and move on or otherwise?

Zan Fleming (00:49:59):

No, keep going and you might get to accelerated disapproval as you turn.

Tim Franson (00:50:06):

Sounds fun. I'll be brief on pandemics. If we look at the climate today from anti-infective risks having come through the covid crisis and with great thanks to Janet and her colleagues for operation warp speed, that was a great illustration of what can be done with appropriate surveillance globally. The collaboration with industry and regulators to deal with the crisis is remarkable and ought to be a case study all our young medical students and pharmacy students have as core curriculum, but we only need to turn around to say with measles cropping up, what therapeutic would we propose using for that? Not anything available, we have our communications embargoed. So most people don't know that in the state of Kansas, one of the largest outbreaks of tuberculosis in America is now occurring with latent and active cases. That's also not very good for children to bridge back reports on congenital Zika having a 14 fold greater mortality in children who come from mothers infected with Zika.

(00:51:21):

We obviously don't have a good treatment idea for that. And we see outbreaks in distressing viral diseases in places like the Democratic Republic of Congo, which appears to be a Petri dish for things like Ebola and now an unidentified viral agent. So as we see a culmination of all this, what we need more than anything else is an early warning system as we would for missiles. And quite frankly, these microbial missiles are coming in through the airways, airplanes and other ways to our country. So if we aren't going to be in the WHO, we need some other way to early detect what kinds of things around the globe could be afflicting our populations in the near term. So not trying to be over amplifying these things, but those are really disconcerting developments and we're not well prepared for any of those potential threats. And I would just close with whether you believe in climate change or not, the mosquitoes are moving northward from the tropics and carrying wonderful things like chicken gunna fever and dengue, also called bone break fever, which for those exposed to mosquitoes in our southern United States are experiencing those things.

(00:52:42):

So I think we can do a much better job at detecting, anticipating and preparing ourselves for those kind of infectious challenges. And I haven't even touched on antimicrobial resistance, which is a problem in war zone areas around the world, especially in children. So quick comment about accelerated approval or disapproval. We also, the report of the Office of Inspector General talking about three of the 24 accelerated approvals that they looked at having issues. And there are certainly issues with that. I have to look at it as, my goodness, 21 out of 24 compounds we're actually positive. What we're doing is right. And you're talking about an over 80%, almost 90% success rate with that, I think we ought to be celebrating it because we would probably do that with normal approvals, although our normal approval rate for lack of withdrawal I think is over 97%. So I think we ought to be very careful about learning from outlier cases and celebrating the mainstream trends that are positive. So back to Anne.

Zan Fleming (00:54:01):

Wow, Tim, what a powerful Cree was. Just inspiring though, very sobering. And we need to be listening to you more often, rather you should be heard widely and all that you say. So can't thank you enough for that. Great summary. Let's now go on to Kelliann Payne, who is our guru for device and diagnostics and the master of CDRH and her practice at Hogan Levels. So Kelliann, take it away. I know you're going to talk about guidances both coming out and maybe going out.

Kelliann Payne (00:54:50):

Thank you. Yeah, I'm a little speechless after the last presentation. But with regard to devices, so my every day today is with the FDA reviewers, the directors of CDRH. And so 2024 was a representative of 2023. Number of submissions were pretty similar. I would say that there's more Novos, there was a little bit of an up jump in de Novos submissions and that could be debated as to why a lot of people think FDA is getting a little more stringent in how they interpret intended use and indications for use. And that they have the de novo pathway now to clean up some of the product codes and inputting devices that would've gone through the five 10 K pathway. And this has been going on, but there was a bit of an up jump in 2024 with de novo submissions. And so that's noted as to why that is.

(00:55:43):

I think with guidances. So there's been a lot of talk on DEI and while there's not been a huge direct effect in the device space, at least not yet, we are seeing some bumps in the road with withdrawing those guidances. Some people, a lot of their clinical utility of their device is based on reaching underrepresented populations. A lot of AI devices are designed for that purpose and having that argument is some teeth as to their clinical utility has kind of put a pause on I would say some submissions, some discussions with FDA on those device types, even breakthrough designation submissions, things of until the dust settles and we see what gets reinstated or not reinstated. I think a lot of are a bit shy to force those arguments and have those discussions with the agency at this point. So I think it's put a pause on some submissions in that sense.

(00:56:34):

The AI guidances came out a lot of finalized guidances on ai. I don't see that changing these finalized guidances as far as what goes into marketing submissions and life cycles of AI devices. I think that will stay the course. I think those guidances simply put into place what we've been seeing from FDA for years and interactions on these submissions with the agency. I actually have some presentations that got put on hold with some organizations and things of the such because they think it may change. I just don't see that for the AI space at least I think FDA has been pretty good about starting to use the PCCP platform, which is the predetermined change control plans. I think when I spoke last year, there weren't as many, we're seeing more and more this year after FDA was kind of given the authority to get those through via the five 10 K pathways and having these interactions and giving more transparency as to what those protocols should look like.

(00:57:29):

So I think that is kind of staying the course at FDA for now. I would say with we see other things in the space. So cybersecurity is a big one for the device space these days with the new requirements put in place in March, 2023 I think it was. And we're starting to see the effects of that. So we're starting to see not substantially equivalent determinations and withdrawals of those submissions based on cyber issues alone. And so it's starting to raise questions as to what is a device, what is a component of a device, can FDA clear software development kits from a cybersecurity standpoint if we can't fully implement the cybersecurity testing required around those. So it's a kind of big one in a lot of people's, I would say

their plan and their business plan and their models are getting a lot of these standalone software development kits through FDA.

(00:58:24):

So that's a pause and I think you're seeing a lot of the digital center of excellence in these discussions coming forward and being asked to join these pre-submission interactions with the agency. We're also seeing fraudulent data issues on the agency side coming out of other countries and FDA's flagging these on the pre-market side. So they're noticing trends when they get these submissions that manufacturers really don't have any insight to because they're just assuming that this data coming from a lab that they paid for such data is appropriate. But what the agency is seeing internally and communicating out is that these reports just look too similar. And so we're having to deal with fraudulent data issues and rerunning of testing and delaying submissions from that perspective. And so there are a lot of the issues we're seeing LDTs remain up in the air. I don't know that anyone knows what's going to happen.

(00:59:19):

I mean I think the clock is ticking for some of the initial requirements and I think it's smart for companies to get prepared for that, at least for the initial few timelines that were laid out for LDTs. So I think that is for me, kind of a summary of where they are on the device side. As far as resources, I would say where we see delays right now are on things like submission issue requests. There's a 21 day timeline for FDA to set up a meeting on some of those submission issue requests. And I would say that's where we're seeing the lag with resources, just getting medical officers in time to get on those meetings or the right technical expertise to attend those meetings in that timeframe. Things like ides with the 30 day timeline continue on course and so do largely five 10 Ks except for these ones with the fraudulent data. I would say once we pass the timeline of FDA's 90 day clock, it kind of goes on forever at that point and there's no real timeline at that point for us then to get back to us on a lot of these submissions. So happy to answer any questions, but the sky's not falling. I would say these are standard issues we were seeing in years past as well.

Zan Fleming (01:00:32):

Well there have been changes in personnel and yet things seem to be going well. What do you see as the overall functional capability of CDRH going forward?

Kelliann Payne (01:00:51):

I mean, like I said, I don't see any major changes. I think we thought it would take a bit of time to trickle down. I think the whole DEI thing kind of hit us a little more by surprise just on the device side and how it impact just even sponsors deciding not to pursue certain submissions at this point in time. So I think just January, that was kind of where the flurry was for us and just pulling back and coming up with strategies to be able to get around and not put so much utility on those DEI arguments if you will. But other than that, for now, I don't see any major impacts. I can't say that they're not coming, but right now it's kind of business as usual.

Zan Fleming (01:01:31):

Alright, well very helpful. Thank you so much. Thank you. Why don't we go on now to Frank Sasinowski whose real passion is rare disease, but you have your fingers and all kinds of things Frank, so you don't have to just talk about rare disease, but the floor is now yours.

Frank Sasinowski (01:01:51):

Thanks Zan. Thanks will start because Kate mentioned about cell and gene therapies made a shout out as part of our wow for cell and gene therapies that maybe we're at the tipping point. So let me just highlight a couple of those. Orchid Kwa HaCo Kirin got approval in March for Len ldi, a drug to treat metachromatic leukodystrophy. It's viewed as being the second curative gene therapy after zol gza for type one SMA. So it's really, it's a good illustration what Kate's talking about the power of gene therapy to be remarkably transformative. And I think we see that, that we continue to see that. Siber OTP under Peter Marks Nicole Verdon also approved a cell therapy, the first mesenchymal stem cell therapy ion cell for treating down to two months of age. Tim was talking about going to pediatrics. This drug, this cell therapy was approved for children as young as two months of old who have acute steroid resistant graph host disease.

(01:02:57):

So I think there haven't been that many cell therapies approved other than part T. So I think to really see OTP and SEBER start to have more traction on what have been more traditional kind of cell therapies, I think it's very encouraging to see cell and gene therapies. I think I agree with Kate and she kind of asked me to speak out to this, so I'm leading off Kate with doing that. The next thing Tim talked about accelerated approvals. So I just want to talk about accelerated approvals for a second because if Tim set up, and that is that I happen to be at, I was honored to be at the conference room, the commissioner's conference room table with Bob Temple when FDA created accelerated approval during the AIDS crisis and nobody today uses a ZT. It is not part of triple HIV therapy. Janet Woodcock was the one who approved the first accelerated approval not for cancer or AIDS when she, in August, 1993, approved beta serum for ms.

(01:04:00):

It was the first drug for ms. Look at how many different classes of MS drugs we now have, right? And then I had the privilege of being with Christie or obedient and Sarepta helping to get the first approval for the first Duchenne muscular dystrophy, DMDA TEIN back in September, 2016. And just this year, the FDA approved another drug for D MD Duat for a thar it's for any boy with DMD regardless of their genetic defect. What am I getting at? Look, the first drug that's approved under accelerated approval doesn't have to be perfect. They sell them off, but they open up, they open up. Academia then gets excited and investment community starts to pour in and stuff. And then we see, look what happened to HIV. I mean it went from a death sentence where not for the FDA coming up with accelerated approval to now being a chronic disease and MS.

(01:05:02):

Beta serum, Janet, Janet, that was a bold step by Janet to take back in August of 1993 to apply accelerated approval somewhere outside of cancer or aids. She did it. And look what happened to MS today and look what's happened to dmd. A lot of people thought the TEON was kind of a controversial approval, but look what it's led to look at how many different therapies we have for dmd. So I just wanted to put a counterpoint to Tim's talking very correctly about DAC accelerated approval. I'm still saying accelerated approval has a lot more utility for advancing public health than we kind of recognize. Lastly, I'll say that a lot of these very rare diseases that we thought could never be cured. Eric Parion, a famous Notre Dame football coach, had children who passed because of Neiman Pick type C. So he started an advocacy and research center at Notre Dame.

(01:05:59):

And this year the FDA approved the first drug for Neiman Pick type C, my Pleva for zebra. And what was interesting about that is that it was approved in September after an August 2nd advisory committee. The August 2nd advisory committee was really important because it was the first meeting of G GEM D,

which is the genetic metabolic Disease advisory Committee. Now Janet Woodcock happened to be at the Willard Hotel in September, 2018. When I, at this every life scientific workshop called for the creation of two things, a standing advisory committee for rare diseases and a rare disease center of excellence. And what we saw in the last year is with the rare hub, the creation of something that's akin to the Rare Disease Center of Excellence. And Amy, Rick is wonderful, great choice. And we saw this genetic metabolic disease advisory can be created, which again, it doesn't have the same title that I call for the rare disease kind of standing advisory, but that's what it is. And so I'm seeing what I'm saying is to everybody out there, whether you're in academia, investment communities, industry, things take time.

(01:07:16):

When I first started talking about flexibility, because I saw how flexible FDA was in approving rare diseases back 25 years ago, and then I had to write a paper on it, and now everybody knows about flexibility. Well, Janet is now talking and Patricia Cone in her exit interview with Biocentric, she talked about ultra rare and how we need a new path. I've been talking about this for a few years too. We need another path. And so things take time. It's going to happen. It's going to happen. And thanks to the leadership of people like Janet Woodcock, she's a gift and a blessing for all of us. So I'll turn it back over to you.

Zan Fleming (01:07:52):

Well Frank, what a great segue to Janet. First of all, I would say what a terrific summary that you just gave us, but it does lead to the opportunity for Janet to react to a number of things that have been said. And so Janet, the floor is yours. I'm not going to try to direct you. I hope you'll mention foods because that is something we like to cover and is very important to our country. But the floor is yours.

Janet Woodcock (01:08:25):

Thank you. Well, first I wanted to comment on something Steve said because, and something Kate mentioned, if the appropriated base is necessary for the FDA user fee programs and they're very close, most of them except for the device one to not having enough appropriations to manage that base, if that base isn't spent, then things go away. And so you could lose the programs if you did a cross the board Kate type of discretionary, federal discretionary budget cut and FDA took a big hit because they just wouldn't have enough money. So because those people are maybe 60, 70% depending on the program supported by user fees, that would be a major blow to the programs and obviously to pharmaceutical development. Now to Frank and Tim's point, I would like to say another thing about accelerated approval, which is in cancer, and I know there's been some concern about that and everything, but if you look at the cancer survival rate in the US over the last decade plus, you see a steady increase in the number of cancer survivors, how long they're surviving their cancer.

(01:09:51):

And this is widely attributed. If you go in the NCI websites attributed to the new therapeutics that are available, and the vast number of those were approved under accelerated approval. So I would say with regard to Inspector General's report and everything, people always want to ding you about something, but you need to look at the results. So like whoever said it, the results for HIV for accelerated approval, the results for cancer with accelerated approval, and we may see the results then for cell and gene therapy for accelerated approvals. So I do think that there need to be voices pushing back because the whole point of accelerated approvals, if they were a hundred percent right, it would be no different than

regular approvals. And so why would we do it? Okay, we're expecting to get this wrong sometimes and it isn't a flaw in the program.

(01:10:50):

It is a foreseeable risk that we're willing to take, but to lower the cancer death rate in the United States to keep people from dying of HIV to advance as Frank said, to advance all these fields and get them moving so that we have treatments for these folk. So those are things I just wanted to say. Now as far as foods, of course people, now I'm a vegetarian and so forth, so I have my own theories about food, but the FDA foods program is highly constrained in its resources and its authorities. So both of those things are highly constrained. Most of the effort is in the field organization because not only are they supposed to inspect domestic facilities there also, which there are millions of 'em, I don't know how many, there's really a lot, maybe 250,000 plus assure imports either by going and inspecting or by certifying that the other country's oversight is adequate of farms and all these things all around the world.

(01:12:04):

I mean this is a gigantic, and then there're supposed to train the state inspectors in the United States and that was part of fedia. So those are things the field has to do. And then oversee imports as they come in of foods and make sure that they're proper imports and they don't have any problems with them. So that's much of the foods program. Then we have the gigantic number of additives, food contact substances, all these things, many of which were originally found to be grass in the 60 seventies. Okay, well science has gone a long way since then, but each one of those is a huge battle. And who's going to generate the data, reliable data to show that say this additive is an endocrine disruptor? Well, FDA isn't funded to do that and frankly, industry is not incentivized to do that type of data. And yet the FDA can't simply go against different food substances based on concern or anecdote.

(01:13:18):

They have to because it's a big regulatory process. I think, and I agree with Steve, it is going to be a giant fight. Are people going to rip Twinkies out of the hands of the voters or pizza or whatever? But I think that just like we did with the OTC monographs, you would have to change the food removal process and so forth to orders, to administrative orders rather than this prolonged often formal rulemaking. That's just a complete nightmare. And don't forget the food program then much of its role is in contaminations like formula or all the outbreaks. So they're constantly responding. The field has to do that too. Do the investigations, figure out what the farm farm caused this possibly and so forth. Not just bacterial but other types of contaminations as well. So the job is enormous and the authorities are pretty minimal. Basically these food substances plus any contamination they can take action and maybe some food labels, right?

(01:14:48):

That's about it. Okay. So I think the diet of Americans is a complicated problem that has caused Aswell knows as endocrinologists, it's caused a tremendous cardiometabolic problem with a huge bunch of Americans. Ironically though, if somebody's against drugging people, okay, the recent weight loss drugs are probably doing more to reverse this than any intervention people have tried to have. But I would say this a cultural issue to some extent about what people eat. And it's also, there's a giant agribusiness out there. Look at all the issues about the front of label warnings where other countries have had those for quite a long time and actually saw, look at the sodium reduction request for companies where we saw reductions in hypertension in countries where they took these seriously and enacted them and the companies had to reformulate their high sodium products too to get to have a healthier product.

(01:16:03):

So I think it's doable, but there's giant cultural forces as well as business forces against this. And also there's a lot of sort of pseudoscience swirling around this. I've talked to a lot of people, like when I was acting commissioner, they called me up and they said it's additives. I'm not sure it's been nailed down. I mean, I think the leading hypothesis is very high caloric density foods that are very easy to consume and cause you to consume more. Maybe some of the additives are harmful, but I don't think it's totally clear. But that's what partly ultra process means. It's easy to consume high caloric density, tasty, have more, have more. So what do you do about that? That's a very interesting question, but you have to, my idea is a doctor is you have to have appropriate diagnosis before you enter onto treatment. And if you really can understand the root cause of the problem, then you might be able to take some action against it.

Zan Fleming (01:17:15):

Well, wonderfully said, we could go on forever with all the different subjects you can cover. I'd ask maybe Dave Fox to come in here and he might pick up on something that you have talked about or take on or be kind of the cleanup man on our issues. And then we'll invite the whole panel to jump in and make this a dinner table conversation.

Dave Fox (01:17:45):

Well, thank you Zan, and it's been just a tour de force just listening to the sweep of issues that we've covered. I'm going to start just building on the least pun worthy statement I've ever heard from Tim Franson, which is what we are doing is, so I think that's such an important anchor for all the swirl of activity that we're ruminating over. And let me just give a little grounding in. What we are doing is, so I usually start off on these hour wows with a review of the prior year. I'm going to abbreviate that, but let me emphasize that. Last year there were 61 novel approvals of drugs and biologics over the last four years. Prior administration on average, 60 new approvals per year, 75% on first cycle review, 66% on some form of an accelerated or priority review path. All PDUFA metrics being met and 68% of the new approvals were new approvals first in the us.

(01:19:04):

So we continue to lead the globe by a long shot in new approvals. That number is hovered around 64 65, we hit 68%. So that's a reminder, a really important reminder of how metrics driven the work of FDA is, how measurable it is. And I think there will be a lot of pressure on the new administration to be in the same zone if not to try to improve upon that. But what I don't think anyone can tolerate, the new administration, the bipartisan support that FDA tends to get on the hill, the public to see those numbers drop because FDA is understaffed and for various reasons unfocused. So that assessment against the metrics is going to come up very, very quickly on the new administration. There is not a lot of time to waste because before we know we'll be getting the 2025 annual report and so on.

(01:20:13):

And then there's the longer term implications of the lag. We could start to see if developers are not getting the kind of quality and timely feedback they need from FDA to plan their programs. So if you don't address this very soon, the slippage will start to be noticed quickly on the annual basis and then over the long-term basis it second, just a reminder of all the various forces in play. So first of all, PDUFA through the end of the 2027 fiscal year through September 30th, 2026 is locked in. So that's unchangeable, as I said. Yeah, F FDA A can miss those metrics. And then it would be an interesting issue as to how the DFA would be renegotiated going forward. But I still am reminded of just how much bipartisan support FDA tends to get and how FDA itself has been, as much as we like to think of it or

have experienced it, each of us individually, I'm sure as some of the most frustratingly stubborn regulators in individual cases.

(01:21:38):

We also know that FDA has been an organization that has undergone enormous changes in our lifetimes. I mean, just to go back to Janet, Janet was not a caretaker of the drug and biologic processes. No, she was a change agent. And we know through the PDUFA process itself, every five years we get new legislation and FDA has adapted to that, not to mention adapting to all the scientific changes. So I think the agency to give it credit is exceedingly good at and experienced at dealing with high pressure, very visible issues with a lot of swirl of social policies, a lot of desperation on the part of families. I mean, you don't get into hotter situations on FDA and what the agency has done, time and again, is gathered itself and reminded itself. It's about the evidence redouble our efforts on focusing on the evidence, let all the other social forces, they'll play themselves out.

(01:22:49):

And I think that that's, if we can focus on that, I think back to Tim's point, what we're doing is right and we have the metrics to ground us. I think we can't control everything, but we can really control and focus on what the agency has been exceptional at, which is focusing on the evidence. The next topic I just wanted to touch on is make America healthy again. I think there is some excitement about now turning our attention to deferring the onset of chronic disease. So a little bit more focus, maybe a lot more focus on WellCare. We've done a great job on sick care for all the reasons we've talked about, all the wonderful gene therapies, cell therapies and products that FDA is approving, but very little historically in the approval area for real true preventive medicine. So make America healthy again, is drawing attention to that.

(01:23:55):

I want to point out that I think that's a sort of a backward looking moniker as if we were healthy in the past and we've become less healthy. I think maybe in the food area there's validity to that. But I want to point out that ARPA H has set as a target in the health span field to increase health span by 20 years, which would make us healthier than we've ever been before. And that's where I am really interested in focusing. And with Z's prodding and leadership of me and Thomas and others, we have drafted some model legislation that we're all very, very excited about to create a, it's more than just a pathway. It's really a categorical shift under the Food Drug and Cosmetic Act for recognizing the concept of a health span claim. This would be health span across all product areas that FDA regulates foods, dietary supplements, devices and drugs.

(01:25:06):

And this would be to create an evidence-based standard in each category that would allow for evaluation assessment of evidence in favor of health span. It's not a linguistic solution like DHE where it's just carefully picking your language. It's rooted in, I think, creating a true evidence standard for health span that is calibrated to the issue of risk benefit in a preventive setting as opposed to a acute treatment setting. So we're very excited about that. I think Zan, maybe you'll talk about this a little bit or Thomas, that we have a program coming up at the end of February to talk about the legislation. As I said, it creates the evidentiary standard across different product categories. It includes incentives, it includes some basis for market. I know there's a lot of concern among developers that the types of products that would be developed for healthspan uses for, because it would be administered pre disease, tend to be products and that have been around for a long time. So how do you incentivize developments and how do you protect your investment? So we've addressed that in the legislation and it includes separately some aspirational monetary prize type approaches for incentivizing and kick-

starting development in this area. And as Janet and Frank reminded us, one of the tried and true techniques in this area is to come up with programs that just kickstart the area. And then we know there's this industry that if you give them a target and you give them an incentive, they'll build a business around it and hopefully we'll all be better off.

(01:26:59):

Last, just to touch on the rare disease topic and the work that Janet's doing. And I've been so privileged to be able to just be deep in the background, just trying to bring the legal perspective to it. I think that, and we talk a lot about accelerated approval and we're talking a lot about super ultra rare disease and how do we solve that problem? And one of the solutions that we tend to gravitate to in this area is some form of conditional approval is loading up the approval with various forms of conditions. And we may have maxed out our tolerance for that. I think we've learned it's certainly suitable in some areas where there is a possible clinical study that could be done down the road, but we make the policy decision that we need to get the treatment to patients sooner rather than later.

(01:27:55):

And that's appropriate in some cases. But in the super ultra rare and the ultra rare, there is really no controlled trial down the road. And once you improve the product, you're not going to get people to enroll in a trial. So we have to just confront that and make contact with that problem and stop trying to go back to, well, we'll just kick the can down the road on the trial. We'll load it up with all sorts of conditions. No, I think that that's what Janet is trying to teach us. And here I am, I should never try to be a translator for you, Janet. You can speak for yourself. But I think what we're trying to do in that area is recognize the value of other tools other than the controlled trial model. And the idea, I think the real shift that we need is to accept that these tools can generate evidence that we consider to be evidence that we consider to be substantial evidence.

(01:28:58):

So in a way, and that's a quibble, it's not so much about a new pathway for rare disease, it's trying to show that under the concept of substantial evidence that we can put value weight on other forms of evidence and call that efficacy, substantial evidence of efficacy, not condition, not loaded up with all sorts of qualifiers, which tend to drive the reimbursement community in anomalous directions, which confuses patients. This would be a true finding of substantial evidence of effectiveness. It would just create put weight on other tools. And I'll let Janet speak to those tools. So we're very excited about that. And I think a workshop is in the works for that, I think February 11th or 12th. But we can certainly share information with people who are interested in that. I saw that come up on the chat

Thomas Seoh (01:29:50):

February 28th. I'll cover it at the end of the webinar.

Janet Woodcock (01:29:53):

This is a different workshop, Thomas. This is different than Thrive. This is

(01:29:59):

The rare disease. No worry. So last, I'll just say I'll close at this, and I shared this earlier. So a long time ago I was in the chief counsel's office at FDA and we would say that we were unbeatable on unreasonable delay cases that we had made the best law on the DC circuit on unreasonable delay. And that was kind of a badge of honor of saying we could withstand any external forces at the agency and we would move at our own pace. And that's a testament I think, to one part of FDA. And as I said, FDA

does it before FDA kind of exists in a duality. And on the other hand, I think FDA is exceedingly capable of absorbing change and responding to the new science and new issues on the ground. And one which we haven't talked about enough is ai. And I think kellyann talked a lot about AI systems built into products and AI product development, but there's also AI in terms of process.

(01:31:04):

And I think one of the things we're going to see very soon is sponsors doing AI generated submissions to cut down on development time. Right now it takes about six months to go from data lock to an FDA submission and AI could really reduce that significantly. And then we can have AI processing on the FDA side of reviews if we can get the budget for it. So we're going to see tremendous change, I think just in FDA processes just because of things like AI and FDA I'm highly confident will adapt to that. So we have this somewhere in between is where FDA exists between their stubbornness, their ability to block out all the noise and their ability to adapt to change. And I think I don't see that changing where they stake out that middle ground. I think what we're doing will continue to be right. So I'm very excited hear about questions and thanks as always Z and Thomas and Connexion for hosting us.

Zan Fleming (01:32:04):

Well, David, that is a lot, very eloquent to start off with and then so many issues to follow. Let's go back to Janet Woodcock and we'll allow her to take and choose a few issues and interact with the other panelists. So Janet, first, thank you so much for joining us and all your contributions, but come back to some issues you'd like to talk about.

Janet Woodcock (01:32:32):

Yeah, well I heard at the RC meeting out in San Francisco, I heard that a firm has used AI to prepare their reports. They were worried, of course, so they did parallel human preparation and then did quality control. They were very surprised to find they had to correct the human reports. And it does cut down on the time tremendously. As I said there though, what I believe is we should stop writing all this deathless prose both on the submitter side and on the agency side. And I tried to get the agency to stop writing all this stuff with some limited success now that we have a short summary basis of approval that everybody contributes to. But then behind it, they still have 300 page monographs from every single discipline. And that's, I think a big time waster. It's like high school, you have to show your work in algebra.

(01:33:37):

So I think we can trust professionals who've, or nine years after college to probably do what they're supposed to do. So that's one thing that I think now, as far as what Dave was saying about the new additional ways to show substantial evidence, I think for rare diseases we can still do, in many cases, we can still do a controlled trial. It's not a randomized controlled trial, though my favorite design is at n of one successive, N of one design where you enroll people early, you figure out their particular rare disease are very heterogeneous, what are their quantifiable problems and what's their trajectory? You follow them for quite a bit of time. Once you get your asset into the clinic, maybe you switch 'em over, maybe you've had them on open placebo to cut down on the placebo effects. We know from Dr. Chu's work that in fact open placebo works and it has a big placebo effect and he's published multiple articles on that which are very compelling. And then you follow those same people. But instead of doing hypothesis testing, which is what the randomized the RCT construct is, you compare before and after successively. And you can keep doing that until you're convinced that the experts, like the statute says, the experts are convinced one way or another have they changed for the better or not.

(01:35:22):

What I want to do is free up people to think about designs and also methods, whatever methods, animal models, whatever, that will give us a totality evidence that would convince experts. And it doesn't have to be, the statute does not say P less than 0.05. It does not call for a hypothesis test type of a controlled experiment. So there are many other ways to control experiments. There are many other kinds of experiments that can be done. And that's why I say it's a technical problem because the RCT construct is not correct for these where you can only enroll 60 people and then you have to p value of lesson 0.05. It's just not going to happen. Usually it's just not going to happen except if you have a miracle cure, in which case you didn't need to randomize anybody. You don't need a statistician. Okay?

(01:36:18):

Right. So why are we doing this? Okay, it's futile and it's causing a tremendous amount of harm friction between the agency, adverse publicity to everybody. It's not a good situation. So we will work on that. And how will the agency do under, my basic concern is that if there is a giant loss of appropriation, that's what I'm worried about, Dave, as far as going on. Because if there is a big cut in appropriations, the user fee programs, I had to manage this budget for 20 years and school people on how these things work. Okay? So I'm very aware of it. If you lose the appropriated base and the drugs programs are very close to that, the drug and biologic, okay, if you lose that, then you can't collect the user fees. You don't have a user fee program anymore. That's how they were set up by Congress. But it's very, to Kate's point across the board things, it's just very tempting to, okay, we'll just take it across the board, make the discretionary budget a lot smaller. Okay, well you can do that, but there will be unintended consequences that could be extremely severe. So those are the two things I wanted to say, Zanne.

Zan Fleming (01:37:38):

Wow. Well, Janet, we thank you for your service. It's just remarkable what you've done over your career. I remember back to the day in the early nineties when you were pivotal in helping us to approve Metformin, which as you recall was a very controversial approval.

Janet Woodcock (01:37:57):

I wish I would like to tell people I wish I had framed the letter I got from public citizen from Sydney Wolf, okay? Because he said if we approve, the world would come to an end. We'd have so many deaths and everything would be terrible and everything. And I didn't save that letter. Of course, we went ahead and approved it anyway.

Zan Fleming (01:38:21):

Well, and we had a strategy and it was to help Sid Wolf understand what we were doing. And we called him the day we approved the product, and long story short, he sort of laid off. And Metformin is now the first line treatment for diabetes, and it's the darling child of the geoscience community for actually reducing risk of multiple chronic diseases. So you've had a hand of just about every part of FDA and we can't thank you enough for that and what a great discussion this has been. We're out of time. I'm feeling very bad that we've not taken questions from the audience as we were intending to do, but we are going to come to a formal close in a moment and people who can hang on around our virtual podium are welcome to do so. We will hope to provide responses to questions in a moment. But Thomas, well first let me just thank all the panelists for a terrific show and we'll just bring the session to a close. But Thomas, give us some last minute instructions.

Thomas Seoh (01:39:40):

Thanks, za. The discussion and questions and chats have been terrific. Again, all registrants will receive the link to the recording within a day or two. And we do want to mention the next free webinar on February 28th by our not-for-profit CATA Institute. Saist is flashing the slide now whose mission is to accelerate the translation of science into public health, to preempt chronic diseases and extend healthy longevity. We will be unveiling the Draft Thrive Act, proposing clear regulatory pathways, appropriate fit for purpose, evidentiary standards as mentioned and incentives for health span products. So please watch your inbox for details with that. The formal portion of this event will close with thanks to the speakers and to you, the audience for your attendance. Another distinctive feature of our webinars Z mentioned is that the virtual hall will be left open for some minutes for those speakers and audience who are available to Terry and chat. So thanks very much.

Janet Woodcock (01:40:36):

Thank you.

Frank Sasinowski (01:40:37):

Thank you. Thank you all.

Zan Fleming (01:40:42):

Well, this was terrific. And wow, I'm sorry that we did not have time for audience questions, but you can still put them in the chat.

Thomas Seoh (01:40:54):

Could I ask a quick question? And you and Steve, what are the odds of the pediatric voucher being extended? What are people hearing and Kate?

Steven Grossman (01:41:06):

Okay, well, I'll step up first. I'm not in the channels where I would hear day to day about these things, but I can respond to the context. And the context is that it's always hard to find a legislative vehicle for what amounts to a small item. I know it's not small item to certain constituencies, but in the big picture of the government it is. So that's always an issue. That's part of what was a problem last year. It's going to be worse context wise before it gets better. This is not going to go on reconciliation, but it does have some very strong supporters who continue to look out for a vehicle that they can just tag it onto. And I don't have any good, maybe the others have a better idea of whether there's something coming up where they think they can add it, but that's the context. It would say based on past, I would say that unless they've got something special lined up, it's going to be four or five months at least before Congress gets to legislation that is more than global reconciliation, budget taxes, immigration

Thomas Seoh (01:42:35):

Z. Do you want to go over some of the questions that were posed?

Zan Fleming (01:42:39):

Well, I was just thumbing through them for the first time and delighted to see a lot of our friends and collaborators across the world and across different domains. Maybe you could pull up a few, Thomas, and we might have a go at them. Those who are still on,

Thomas Seoh (01:43:01):

I don't know if the posters are still on. You can see our participants and Zen, if you see some people you want to pluck out and call out, please feel free to do that. But I think one question was what are the implications of the US withdrawing from WHO? That's not so much regulatory or FDA, but it's public health. So I see Tim kind of reaching forward. Kate nodding along.

Tim Franson (01:43:26):

Sure.

Zan Fleming (01:43:26):

Tim, go ahead.

Tim Franson (01:43:28):

There are certainly several considerations. One is the surveillance capabilities that does this potentially compromise us as a country for getting prompt information about new infectious trends. That's certainly a great concern to the Infectious Disease Society of America and other groups that I'm familiar with. The other thing would be there's the speculation that as America drops away from that and it's fiscal commitments, who will take a dominant view and will, whatever that party is, that could be China,

Zan Fleming (01:44:11):

It will be China, what

Tim Franson (01:44:13):

Would happen to US interests for even any collateral access to surveillance.

Zan Fleming (01:44:18):

And

Tim Franson (01:44:19):

A lot of the research that goes on as it relates to antimicrobial resistance and so forth usually comes out of W-H-O-C-D-C type collaborations. It would be very unfortunate to see those things suffer as a result of broader policy concerns.

Zan Fleming (01:44:37):

Yeah, it's a terrible development.

Janet Woodcock (01:44:40):

I want to mention a very prosaic aspect of this question. So this is going deep, deep into the weeds, the other direction from where Tim is taking us, I think on the surveillance infectious disease, it's just the issue is just hard to even put words to. But WHO also administers some very focused programs like the international non-proprietary naming. So getting into things like nomenclature, which what could be more boring, but nomenclature is at the heart of consensus worldwide standards. And so when new molecules, new Moes are developed, you apply to the WHO through their INN program for the assignment of a name, and that becomes hopefully the universal name around the globe. And that

serves some very obvious purposes. And FDA is on that panel, they're asked their views, and because we pay the largest fee, we tend to have the largest voice. And now we are buying our way out of being the most influential voice at the table for things as broad as, yes, the detection of disease, but also things as mundane as the vocabulary that we assign to all the new things that we're developing.

Zan Fleming (01:46:02):

Great point

Thomas Seoh (01:46:03):

Z. You see a question from Kelly Close and from David in the chat?

Zan Fleming (01:46:08):

Yeah, well, it's great to see those messages and we'll certainly get back to 'em. Dave, I know you're going to get a lot of questions about the Thrive Act, and if you could put that slide up ef, we might just mention what the Thrive Act is. You can see down there, the footnote is that it's the Therapeutic Health Span Research Innovation and Validation Enhancement Act. And that I believe is a much better way to name this visionary legislation than what our original prosaic term was. The Health Span Act. Health span is a topic that is somewhat understandable, but it has different interpretations. But I think Thrive has the connotation of just what we're wanting the people, our fellow citizens in the United States and across the world to do. And that starts with preventing multiple chronic diseases and age related disabilities. So David, you have been amazing in articulating this draft legislation and stay tuned for the discussion of it.

Steven Grossman (01:47:47):

We're, if there are more questions than this, otherwise, I wanted to go back to WHO for just a second

Zan Fleming (01:47:53):

Please.

Steven Grossman (01:47:53):

Which is that there's a different view that's not inconsistent with what was said. And a lot of these, especially the international initiatives that are kind of in your face, it's really clear the plan is at least on some of them to use as a negotiating tactic. And so while I think we should be appropriately concerned, as people have said about the departure from WHO, I think there's a good chance this one's going to be okay. Some other countries are going to have to provide a larger portion of the budget and we'll get some leadership that we like better than the current leadership, but that the end game is not necessarily actually withdrawal. It's a hypothesis.

Zan Fleming (01:48:48):

Okay, well that's encouraging. Let's hope that that turns out to be the case.

Thomas Seoh (01:48:53):

Is there an effective date for the withdrawal like in June? Did I read that correctly? I did not see that one way or another.

Zan Fleming (01:49:01):

Well, I spent a year and a half at WHO, and I can say that there's an awfully lot of good that it does. There may be, there definitely is room for improvement, but it's such an important organization for humankind.

Steven Grossman (01:49:24):

I am pleased to give you an optimistic interpretation, and I hope I'm proving correct.

Zan Fleming (01:49:31):

Well, you do bring the broad view of the sweep of history, and that is somewhat reassuring or it is reassuring, not somewhat. It is reassuring.

Thomas Seoh (01:49:42):

Can I ask sort of a party favorite question among the panelists, what did you hear from other panelists that surprised you or you learned something that is important as a takeaway?

Steven Grossman (01:49:55):

Well, I'll go with that one because Janet spoke to something that's in my bail, which is the maintenance of effort and the relationship between the triggers for user fees and appropriations. And it surprised me because the last time I looked at it a couple of years ago, it looked like there was plenty of room for the appropriation numbers to come down without triggering the maintenance of effort and collapsing the user fee programs. One on my notes is to go back and talk to Carter Esham, who's the new head of the alliance for a stronger FDA, and look into where we are with regard to those thresholds because maintenance of effort was very important in the creation of the user fee programs. That is industry bought in part on the idea that it was not going to replace congressional support, that it was additive. And if anybody in the administration or elsewhere is under the illusion that by collapsing the appropriation that they're going to turn it into an industry paid agency, which is bad on a lot of other counts, but it's just not true because the maintenance of effort provisions then at a certain point, if you're not putting enough into appropriations, you don't no longer have legal authority to collect the user fees.

(01:51:25):

And so on the one hand, in my bail wick, on the other hand, I wasn't focused on it. And I think that was a really important point that Janet made. We'll go back and through the alliance for a stronger FDA, I think we'll have some comment in the next few weeks or whatever, I hope as to how close we are on those thresholds.

Janet Woodcock (01:51:46):

I thought from Kate's presentation, I'm reminded of how hard it is to figure out what the coherent policy is of the incoming administration and the nominee for HHS. So for example, on this user feed point, I've seen chatter among some people in the incoming administration that they believe FDA should be operating on warp speed all the time. Why should warp speed be reserved just for vaccines? And they don't have vaccines. Why don't we have warp speed for cell and gene therapy and everything else? Exactly, Steve. Exactly. So you have this tension between you have one camp railing against the pharmaceutical industry capturing FDA through payment of user fees. And so we have to get the pharma industry out of FDA financially. But on the other hand, we want FDA to have the resources to be

on warp speed all the time and how the kind of polar opposites are going to be reconciled. Nobody knows.

Steven Grossman (01:52:57):

Yeah, and I have another one that I've talked some about, which is I, Kennedy was talking about how the agency was under the control of industry and we needed to get user fees and other things and make the agency more independent. And at the same time, and I am never able to pronounce his last name, unfortunately, is talking about how the agency is impeding innovation in the industry. I don't know any way to reconcile those two views. Either the agency is captured by industry or it's a hindrance to industry. How can it be both? So yes, it's not one or two or it's five or six or seven types of contradictions as you come in and you have very strong people, and I think it plays a role that they're moneyed people and they're used to the idea that you invest in something. I foresee there may be a break with the whole concept of innovation between what might be called the Silicon Valley model of innovation, which is move fast and break things.

(01:54:20):

And oh, by the way, if it's a good idea, you can be on the market in 18 months or less. 18 months is slow. And the biopharmaceutical concept of innovation, which pleads to certain patients, which has standards that have to be applied, and there's potentially conflict over trade, over ip, over the value of regulatory process. I don't know. But I mean if we're talking about contradictions that they're going to have to be resolved or maybe they'll go on and just fuddle people. There are plenty in the current team of people who have influence in this administration.

Zan Fleming (01:55:02):

There is cognitive dissonance for sure. Go ahead, Kate. And then I want kellyann to comment on the fact that CDR H and devices diagnostics did not attract a lot of discussion today. Maybe that's a sign of success.

Kate Rawson (01:55:21):

I was just going to make a couple quick points to what Steve just said. Move fast and break. It works really well in the tech industry. You don't have people's lives at risk. And so that's one thing to think about there. The contradictions also strike me. The obvious one is we need to reduce the influence supposedly that industry has over FDA by reducing user fees, but at the same time, we want to cut $2 trillion out of the federal budget. So I don't know how you match those things either. And then the last thing, the thing that really struck me was Janet's comments and Steve's comments about the resiliency of FDA to move through change, which I agree with, but also reflect on the fact that FDA is individuals too, and each one of those individuals is being impacted by this transition in different ways and reacting to that in different ways. And so yes, the agency as a whole is resistant and the laws are there to protect it, but I have a lot of feelings for the individuals that work there because it is an uncertain amount

Zan Fleming (01:56:27):

For sure. Well, kellyann, is the device realm just a different paradigm for engineers than physicians? I mean, it seems that everything is going pretty well at CDRH.

Kelliann Payne (01:56:49):

I guess from where I stand and what I do on a day-to-day is I interact with a lot of the lead reviewers deep in submissions. And so I would say from that perspective, I don't see a lot of change. Not yet. I mean, we're day what into the administration, and so I just haven't seen a lot of it trickle down and we didn't expect to see a lot of it right away. I would say on the device side, again, I think a lot of what we've seen is things written down in guidances that we've been seeing forever. I mean, they've been upping the ante on AI in diagnostic and therapeutic spaces. The data required, I do probably 50% of what I do day in and day out is AI based. And so they want subgroup analysis, they want more data. I don't see any of that changing.

(01:57:33):

I don't see any of the requirements necessarily changing again, like diagnostics, LDTs. I mean that's been a topic of conversation for a long time and we just don't know what is going to transpire there. So I don't have a crystal ball on that. Again, I think time is ticking and you should get ready for it. But I guess if there's questions on specifics, I know there was a question regarding how they would use the ING K and de novo pathways versus pressure away from PMA devices. Again, I don't see that. I think FDA has always used a risk-based approach when they're regulating devices, and that is not going to change. I do think de Novo gives an opportunity for strategy as to how you're going to position your device, what you're saying about it, what are your indications for use? Are you biting off this huge diagnostic therapeutic claim and going PMA, or are we going to take a step back and take an initial step and get some type of low to moderate risk de novo claim?

(01:58:29):

And so that's a strategy a lot, I would say, for devices and we just have to work through that. But you do see the de novo space being used more and more. I mean, when I started that was a black hole. Now they don't scare me. I think people and investors shy away from de Novos because of the success rate. But I think that's simply that they haven't had the early conversations with FDAA lot of times. And that the standard that's used of, does my benefit outweigh my risk, is a bit subjective. And you really have to have a strong argument going in. You have to have every piece of data at your resources, patient preference data, everything you can get to build that benefit risk discussion. So I guess it's where I see devices coming out, and I'm always happy to answer specific questions because each device type and each space is different.

Zan Fleming (01:59:17):

Well, clearly it keeps you very busy. So that's a good thing. And I see, Tim, you have your hand up and then Dave raised his hand.

Tim Franson (01:59:28):

Sure. Thanks Dan. Just a thought that I had wanted to bring up during the general discussion and be interested in my colleagues' assessments, but I was concerned by the HHS secretary candidate's comment about committees being sock puppets for the industry and the concern being that that may have a chilling effect on the recruitment of advisory committee members. So we just need to be cognizant of that. I think that would be an unfortunate unintended consequence.

Zan Fleming (02:00:01):

Yeah, yeah, so true. And these kind of effects are just going to have no end and the kinds of havoc they can wreak. But let's hope that Steven's view is ultimately the right one. Things will work out if we just stay calm and carry on.

Tim Franson (02:00:29):

Stay calm, carry on and pass the butter

Zan Fleming (02:00:34):

Or the guns. Go ahead, Dave.

Janet Woodcock (02:00:39):

Well, yeah, as a lawyer here, I'll bring us back to first principles. So this is Yao or Wow or holy cow. So I have Yow. Wow. Holy cow. Question for kellyann and maybe others, which is, so what do we make of Elon Musk being regulated by CDRH with his Neuralink?

Zan Fleming (02:00:59):

Oh, that's a good

Janet Woodcock (02:01:01):

One. How do we even begin to make sense of that?

Thomas Seoh (02:01:05):

You're on mute kellyann

Janet Woodcock (02:01:08):

Intentionally. I think I would mute myself as well.

Kelliann Payne (02:01:15):

Sorry, I'm just like, yeah, there's nothing coming out. Yeah, I was not muted on purpose, but yeah, I don't know. I don't know. I have a good response to that. Dave,

Janet Woodcock (02:01:28):

Melissa King in the chat has a good response

Kelliann Payne (02:01:31):

Regulated. Yeah.

Zan Fleming (02:01:33):

Yeah, I think that's a great idea. He should be regulated as a device and A PMA should be

Janet Woodcock (02:01:41):

Required. Well, I mean, he is right? I mean, he's being regulated by CDRH. Yeah, he was on clinical hold for a while, I think, right?

Kelliann Payne (02:01:50):

Yeah.

Janet Woodcock (02:01:50):
Or Neuralink not,

Kelliann Payne (02:01:52):
Yeah,

Zan Fleming (02:01:53):
I'm talking about him.

Kelliann Payne (02:01:55):
Oh, human

Thomas Seoh (02:01:58):
As a medical device. Oh, okay.

Kelliann Payne (02:02:04):
Yeah, it was on hold. It was a breakthrough designated device. But yeah,

Kate Rawson (02:02:12):
There was a question in the chat about what we thought of our nominated FDA commissioner, and we didn't talk too much about McCarey, so I just wondered what everybody thought. My take on it is he's a more traditional pick than RFK Jr. I think we can all agree to that. He's not just to name names, he's not a Scott Gottlieb by any stretch. And I had sort of posited to this group before this webinar that he might be more of a high profile Steven Hahn in that he's an academic, he's got sterling credentials, but unlike Rob Kayla or Scott Gottlieb, he doesn't have real knowledge of FDA, which isn't necessarily bad. It doesn't mean he would be necessarily ineffective or dangerously influenced, but there's certainly been other commissioners that don't have that kind of background to FDA, even very effective ones like Mark McClellan that came to FDA with very little understanding or little understanding of the inner workings. And even Scott, when he came to F fda, a had no knowledge of foods. Janet had no knowledge of foods when she started and you got to drink the fire hose or whatever that term. So politically, he's a good fit. He's critical of vaccine mandates. He, like Kennedy, thinks that there is a crisis with over medicalization, particularly in children. So that's sort of my, I can't wait for those hearings, but I wonder what everybody else thinks too.

Zan Fleming (02:03:57):
Well, and what about the timing? Steven has already declared that he is qualified April

Thomas Seoh (02:04:02):
One.

Zan Fleming (02:04:04):
April one.

Thomas Seoh (02:04:04):

Steve said

Zan Fleming (02:04:07):
In the meantime,

Thomas Seoh (02:04:08):
What's the over under?

Zan Fleming (02:04:09):
Yeah, do you think that he will be on board by mid-April? Yeah,

Steven Grossman (02:04:18):
I still stick with that. But Kate for one, as a reporter, follows this through different people. Is that a good number for a rough estimate that

Thomas Seoh (02:04:32):
Kate, I can also say that at the CY Summit, I can't remember who said this, but they noted that McCarry has been a, I don't know critic if that's the right word, critical of some issues with FDA, but they've tended to be in the bucket of safety. So if there are initiatives, and I don't know what that does, Tim, for initiatives in pediatric products, but so long as the focus is on being sure that sure is not the right word. It's no one bats a thousand, that if you don't have some failures, maybe you're not innovating hard enough. But that's a direction where it's not necessarily harmful to the mission of the agency. Keep people safe is a band. It's a balancing act. And otherwise he seems to be within the band, as you mentioned. I'll shut up here.

Janet Woodcock (02:05:31):
Hey, did you say he's, he's known to be pro-choice?

Kate Rawson (02:05:35):
That was,

Thomas Seoh (02:05:36):
I did not say that.

Kate Rawson (02:05:38):
I said that I thought he was pro-choice, but that could be.

Janet Woodcock (02:05:43):
We want to check. I think we might want to, yeah, let's put a pin in that and check.

Kate Rawson (02:05:46):
No, no, no, I'm sorry. He's not, he is not pro-choice. Yes, he's aligned with Trump in that and anti, yeah,

Steven Grossman (02:05:58):

He does not raise the same issue in that regard as Kennedy does of having flip flopped.

Thomas Seoh (02:06:05):

Can I ask, oh, I'm sorry, Steve, go ahead.

Steven Grossman (02:06:07):

I was just going to add one of the thing, Kate, we made some comparisons to other people, but I have very specific memories. After Obama came in and nominated Peggy Hamburg, who was a great FDA commissioner, and I had at least a half dozen calls from people in the farm industry who were very anxious, very upset. She wasn't a pharma or a biomedical researcher type. So when you start actually counting up the CLIs and the people who have been biomedical researchers, they're actually the minority until you go back to the 1970s with Don Kennedy. So that's maybe part of why I'm saying there's really, to me, there's no credential reason. If you look at the variety of backgrounds for people who've been commissioner, I would say the one, if anything, he's never run a large organization, but even that wouldn't hold for all the people who've been, commissioner fact that was a strength of Peggy's was that she run the New York State City Health Department.

Kate Rawson (02:07:23):

And just to put a point on it, he is pro-life. So thank you.

Thomas Seoh (02:07:28):

Can I ask the $64,000 question in this dinner salon context, nobody is ringing hands or pulling out hair, but the canary in the mine is with Pistone. Does the fact that the commissioner has that particular belief, does this particular panel think that it's going to affect how a drug that's been approved for other purposes than abortion and it's been around with decades of data, might that be dealt with a different context or standards than before? I'm just asking the question.

Steven Grossman (02:08:12):

Every commissioner faces those things. We just have more of a sharp alignment in our society on abortion, et cetera, so that it stands out more. But I'll go back to what I said. I don't think that he himself probably knows if he's asked to do something that he feels is not in the best interest of people, when does he say no? When does he try and find a compromise and when does he just go along with the crowd? Every one of us who have been in government have faced that, and it's a big question. It's not in the least solo to him or his predicaments or his views.

Tim Franson (02:08:57):

I think the only thing that caused me at least some concern is his prior publications on the Orphan Drug Act and that they represented windfall to industry. So I would imagine that will be one of the questions. And those pieces are from eight years ago, so perhaps they're not representative of his current position.

Steven Grossman (02:09:21):

I had not seen those. And having been in and out of the orphan drug thing since the beginning, usually it's a matter of presenting that because I think it's a very easy position, particularly for pharmaceutical critics to come to that somehow it's wrong to put so much energy and attention into the few at theoretically the expense of the many. And that when you actually get down and say, what happens?

Why are they doing this? What breakthroughs come out of it? What are the advantages that a robust program in orphan drugs has brought about? I think at least I can't think of anybody who wasn't sufficiently convinced. So I had not heard about that, but I would be optimistic on that point.

Tim Franson (02:10:10):

Yeah, I just think it would be something.

Steven Grossman (02:10:13):

Nord has done a couple of very good studies on this as well.

Tim Franson (02:10:16):

Oh, of course. I just think it'll be one of the likely questions at the hearings, and if

Steven Grossman (02:10:23):

I nor, I would certainly want it asked,

Tim Franson (02:10:27):

And I'm afraid I'm going to need to run now. But I

Zan Fleming (02:10:29):

Love these things once a year, so why don't we bring it to a close and we thank our audience a good part of it for staying on, horrific to have you, and we'll see you next year, if not sooner, maybe even four weeks from today when we bring back the Thrive

Tim Franson (02:10:50):

Act. Holy cow. Thank

Zan Fleming (02:10:52):

You. Yeah, it's a holy cow. Thanks.